## REMARKS

After entry of this Amendment, Claims 1, 3-7, and 9-18 will be all the claims pending in the application. Claim 1 has been amended to incorporate the features of Claims 2 and 8, and to delete the recitation "or lowering temperature." Claims 2 and 8 have been canceled. Claim 3 has been amended to remove its dependency from canceled Claim 2.

No new matter has been added.

Entry of the above amendments is respectfully requested.

### I. Preliminary Matters

Applicants thank the Examiner for withdrawing the the rejection of Claims 1-9 under 35 U.S.C. § 112, second paragraph and the rejection of Claims 1, 2, 7 and 8 under 35 U.S.C. § 102(b) over Nelles et al. (U.S. Patent Publication 2002/0095219) in view of Applicants' Amendment filed October 30, 2008.

### II. Claim Rejections - 35 U.S.C. § 112

On page 3 of the Office Action, Claims 1-9 and 18 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to reasonably convey to a skilled artisan that the inventors had possession of the claimed invention at the application filing date.

Initially, Applicants submit that Claims 2 and 8 have been canceled, rendering the rejection moot for these claims.

In response, and while not admitting that the rejection is appropriate, Claim 1 has been amended to delete the limitation "or lowering temperature," thereby rendering the rejection moot.

Withdrawal of the rejection is respectfully requested.

**III. Claim Rejections - 35 U.S.C. § 103**

A. On page 2 of the Office Action, Claims 1-9 remain rejected under 35 U.S.C. § 103(a) over Nelles et al. in view of Kobayashi et al. (U.S. Patent No. 6,294, 313) and Georger et al. (U.S. Patent No. 5,324,591).

Initially, Applicants submit that Claims 2 and 8 have been canceled, rendering the rejection moot for these claims.

In response, and while not admitting that the rejection is appropriate, Claim 1 has been amended to incorporate the features of Claims 2 and 8. Applicants respectfully submit that present Claim 1 is patentable over the cited documents for the following reasons.

Applicants submit that a *prima facie* case of obviousness has not been made because the Office Action has not identified a reason why a person of ordinary skill in the art would combine the disclosures of Nelles et al. with the disclosures of Kobayashi et al., Georger et al., or Haddow et al.

The Office Action contends that Kobayashi et al. and Georger et al. disclose the use of siloxane as cell adhesion materials, which would not require enzymatic dissociation treatment to release the cells from the substrate. However, Nelles et al. discloses that the technique for attaching and patterning biomolecules on a surface using polydimethyl siloxane (PDMS) uses dissociated cell cultures, are of limited use, and does not permit full control and guided cell attachment and growth on surfaces. *See,* paragraphs [0006]-[0007]. Accordingly, Applicants submit that Nelles et al. disparages and teaches away from the use of siloxane as a cell adhesion molecule and thus, a skilled artisan would not have a reason to look to the siloxane disclosed in Kobayashi et al. and Georger et al. in combination with the method disclosed in Nelles et al. with a reasonable expectation of success.

Further, a skilled artisan would not have a reason to combine the disclosures of Nelles et al. with that of Haddow et al. The Office Action admits that the enzymatic degradation disclosed in Nelles et al. is based on the use of collagen or fibrin-gel as cell adhesion molecules. However, Haddow et al. discloses several disadvantages for the use of collagen as a substrate for culturing skill cells and transferring them to a wound bed:

> For example, collagen has to be prepared, typically from a cadaver, which takes time and expense. Moreover, it is important to completely de-cellularise the collagen to reduce immune rejection and the likelihood of transferring infectious agents to the recipient of the donated collagen. Methods to sterilise collagen-containing tissues are known in the art but many result in a collagen base which lacks the consistency of native collagen. There is therefore a need to develop new substrates which support cell proliferation and transfer to a wound bed to promote wound repair.
>
> (*See*, page 2, lines 11-19).

Accordingly, Applicants submit that Haddow et al. disparages and teaches away from the use of collagen as a cell adhesion molecule and thus, a skilled artisan would not have a reason to combine the method of forming a pattern of cells on a surface using collagen as the cell adhesion molecule disclosed in Nelles et al. in combination with the method disclosed in Haddow et al. with a reasonable expectation of success.

Applicants thereafter submit that Claims 3-7 and 9 are at least patentable over the cited documents by virtue of their dependency from Claim 1.

Withdrawal of the rejection is respectfully requested.

B. On page 5 of the Office Action, Claims 1-9 and 18 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Nelles et al., in view of Kobayashi et al., and

Georger et al., and further in view of Haddow et al., and Ostuni et al. (U.S. Patent No. 6,893,850).

Initially, Applicants submit that Claims 2 and 8 have been canceled, rendering the rejection moot for these claims.

In response, and while not admitting that the rejection is appropriate, Claim 1 has been amended to incorporate the features of Claims 2 and 8. Applicants respectfully submit that present Claim 1 is patentable over the cited documents for the same reasons discussed above in section III.A.1. That is, a skilled artisan would not have a reason to look to the siloxane disclosed in Kobayashi et al. and Georger et al. in combination with the method disclosed in Nelles et al. with a reasonable expectation of success, and a skilled artisan would not have a reason to combine the method of forming a pattern of cells on a surface using collagen as the cell adhesion molecule disclosed in Nelles et al. in combination with the method disclosed in Haddow et al. with a reasonable expectation of success.

Applicants further submit that present Claim 1 is patentable over the cited documents for the following additional reasons.

Applicants submit that the Office Action asserts that that since Kobayashi et al. teach a substrate having a layer comprising a photocatalyst and a material having varying wettability through the action of photocatalyst, it would have been obvious for the person skilled in the art to replace the substrate of Nelles et al. with the substrate of Kobayashi et al. The Office Action also asserts that since it is well known in the art to utilize photolithography for forming a high definition pattern and the pattern-formed substrate has been utilized for cell culture according to Georger et al., the above-described replacement is suggested.

Applicants submit that the method of Nelles et al. requires transferring the matrix in which cells are embedded, and the cells are damaged when removing the matrix adhesion from cells. Therefore, Nelles et al. cannot provide the advantageous effect of the present invention, that is to arrange and culture cells in a fine pattern without damaging them.

Applicants also submit that Georger et al. teach a method wherein a substrate having a layer of EDA (N-(2-aminoethyl-3-aminopropyl)-trimethoxysilane) is exposed to form a pattern and cells are inoculated thereon to form a cell pattern. However, Georger et al. do not teach or suggest further transferring the cell pattern. Instead, Georger et al. disclose only the cell array substrate of the present invention and do not disclose the cell culture substrate of the present invention. On the other hand, the characteristic feature of the present invention is the combination of the cell array substrate and the cell culture substrate. Though a cell pattern can be formed on the substrate as disclosed by Georger et al., Applicants submit that it is impossible to culture cells to cause differentiation and tissue formation on the substrate. By transferring a cell pattern formed on the cell array substrate to the cell culture substrate, it becomes possible to culture cells to cause differentiation and tissue formation on the substrate. And by employing the water contact angles between 10° and 40° as required by present Claim 1, the cells can be easily transferred to the cell culture substrate in a patterned state without damage.

The Office Action states that Haddow et al. teach direct contact of cells on a patterned substrate to another including tissue or organ; thus a person of ordinary skill in the art would have been motivated to transfer cells on the patterning substrate to another target. However, Applicants submit that Haddow et al. do not teach or suggest that cells are promoted to differentiate and form tissues when they are arranged in a pattern. Therefore, Haddow et al. do

not mention anything about forming a certain 2-dimensional pattern which is advantageous for the tissue formation of cells.

The Office Action states that that Kobayashi et al. teach that the surface having high critical surface tension would have the wettability in terms of contact angle with water being not more than 40°. However, Applicants submit that the method of Kobayashi et al. is directed to a process for producing a lens, which is in a completely different field from the method for culturing cells. Further, Kobayashi et al. do not teach that the contact angle of not more than 40° is advantageous in transferring cells.

The present invention was made in view of the following problems in culturing cells in a patterned state to promote differentiation and tissue formation of the cells. A high-definition pattern can be obtained when patterning is carried out by a photolithography method or the like using a photosensitive material. In such case, however, a cell adhesive material should have photosensitivity. Chemical modification of a biopolymer or the like to impart such photosensitivity is often difficult. This leads to a problem such that the selectivity range of a cell adhesive material is extremely narrowed. A photolithography method using a photoresist requires the use of a developing solution or the like that may adversely affect cell culture. Moreover, biomaterials and the like having high ability to culture cells are generally difficult to decompose by plasma. Thus, patterning using a plasma etching method also has low industrial productivity and thus is impractical.

When cells are adhered to a cell array substrate with a water contact angle between 10° and 40° and then transferred to a cell culture substrate, the cells can be caused to adhere to a cell array substrate in the form of a monolayer. From there, the cells can be easily transferred to a cell culture substrate because of weak adhesiveness to the cell array substrate. The present

invention enables the arrangement of cells in a fine pattern and the culturing of the cells in a patterned state thereby promoting tissue formation. Applicants submit that none of the cited documents, as discussed above, teach or suggest that cells can be transferred without damage by using the combination of the cell array substrate and the cell culture substrate and adjusting the water contact angles of the cell array substrate. Further, since the method of Kobayashi et al. is in a completely different field from the method for culturing cells, a person skilled in the art would not have been motivated or would not have a reason to replace the substrate used in the method of Nelles et al. with the substrate disclosed by Kobayashi et al.

Applicants thereafter submit that Claims 3-7 are at least patentable over the cited documents by virtue of their dependency from Claim 1.

With regard to Claims 9 and 18, Applicants submit that Ostuni et al. do not make up for the deficiencies Nelles et al., Kobayashi et al., Georger et al., and Haddow et al. with regard to present Claim 1 as discussed above, and therefore a *prima facie* case of obviousness has not been made because the cited art combination does not teach or suggest each and every element of the present invention.

Withdrawal of the rejection is respectfully requested.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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